

Restoring vision by sheet transplants of retinal progenitors and retinal pigment epithelium (RPE) derived from human embryonic stem cells (hESCs)

Grant Award Details

Restoring vision by sheet transplants of retinal progenitors and retinal pigment epithelium (RPE) derived from human embryonic stem cells (hESCs)

Grant Type: Early Translational IV

Grant Number: TR4-06648

Project Objective: To differentiate hESC into optic cups and further into sheets of photoreceptor progenitors (>80%) together with hESC-derived RPE; and develop mature photoreceptor cells that integrate with the host after transplantation into immunodeficient RD rats and demonstrate a functional change in vision

Investigator:

Name:	Magdalene Seiler
Institution:	University of California, Irvine
Type:	PI

Disease Focus: Vision Loss

Human Stem Cell Use: Embryonic Stem Cell

Cell Line Generation: Embryonic Stem Cell

Award Value: \$3,998,948

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Reporting Period: Year 4/NCE

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Grant Application Details

Application Title: Restoring vision by sheet transplants of retinal progenitors and retinal pigment epithelium (RPE) derived from human embryonic stem cells (hESCs)

Public Abstract: There is currently no effective treatment to restore or improve vision for patients suffering from incurable blinding diseases such as dry age-related macular degeneration and retinitis pigmentosa, which need both new photoreceptors and retinal pigment epithelium. However, a unique method to transplant fetal retinal progenitor sheets together with its supporting retinal pigment epithelium (RPE) has been shown to improve vision in animal models of retinal degeneration and in patients. Differentiation of human embryonic stem cells (hESCs) into sheets of retinal progenitor tissue that contain photoreceptor progenitors and RPE cells could create an unlimited supply of donor tissue. Our lab has generated retinal progenitor tissue from hESCs in 3-D constructs ("layers"), and a new immunodeficient model of retinal degeneration. Recently, several laboratories have shown that hESCs can "self-assemble" into early stages of eye development and develop into laminated structures. The hypothesis of the proposed project then is that hESCs can be consistently differentiated into sheets of retinal tissue, which can restore visual responses after transplantation to a new immunodeficient rat model of retinal degeneration that does not reject human cells. In the final year, we will standardize methods to increase the production of these sheets in a way that complies to good manufacturing practice. This project will ultimately help to restore vision in patients suffering from retinal diseases.

Statement of Benefit to California: Retinal diseases reduce the quality of life of patients who suffer from vision loss and at significant cost to the health care system. Age-related macular degeneration (AMD) destroys the central vision and is the most common cause of blindness among people over 65. In 2010, AMD affected 2.1 % of the general population which means 2.1 million in the U.S. and about 240,000 in California, with these numbers projected to grow to 5 million (in the U.S.) in 2050 as the population ages. Ca. 20-35% of AMD cases develop irreversible geographic atrophy with local loss of RPE and photoreceptors in the macula. Another incurable disease, retinitis pigmentosa (RP) which is inherited (1:3500) and occurs in younger people, affects the light-sensing photoreceptors first, but also the supporting RPE layer beneath the retina following photoreceptor degeneration. Thus, both AMD and RP patients will need both new RPE and photoreceptors. The proposed replacement therapy is the only one that targets more mature disease stages of both AMD and RP, for which no other therapy exists. An effective treatment will keep afflicted individuals productive, enhance State tax revenues and defray the healthcare cost burden to taxpayers. It will also lead to robust industry developments in the fields of clinical transplantation, drug screening, and predictive toxicology, effectively leading to job creation and tax benefits to the State as a result of consumption of research and clinical goods and services.

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